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WOMBLE CARLYLE SANDRIDGE & RICE, PLLC
ATTN: PATENT DOCKETING
P.O. BOX 7037
ATLANTA, GA 30357-0037

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NIEBAUER, RONALD T	
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10/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/792,376	SABETSKY, VLADIMIR	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-37,41 and 43-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-37,41,43-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 8/10/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously (11/3/06) applicant elected Group II with traverse. Due to applicants amendments an additional restriction requirement (election of species) was mailed 8/5/09. Applicant's election of recombinant human insulin in the reply filed on 12/30/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

As discussed below, the elected species was found in the prior art or rejected in a 103 rejection. In accord with section 803.02 of the MPEP, the claims have been examined fully with respect to the elected species but the search has not been unnecessarily extended to all species. Any art that was found in the course of searching for the elected species that reads on non-elected species is also cited herein. As such, claims 27-37,41,43-51 are under consideration.

Claims 1-26,38-40,42 have been cancelled.

Claims 27-37,41,43-51 are under consideration.

Claim Rejections - 35 USC § 112

Claims were previously rejected under 112 2nd. Since the claims have been amended the rejection is updated to correspond to the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-37,41,43-45,47,49,51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 43-45 and dependent claims 27-37,41,47,49,51 recite 'recombinant'. The specification (page 26 section 0070) defines recombinant to refer to 'combinatorial library of molecules which may be further processed into another state'. The metes and bounds of the claims are unclear. Section 2111.01 IV of the MPEP states that applicant may be their own lexicographer but should set forth definitions with clarity, deliberateness, and precision. In the instant case, the definition of recombinant is unclear. The art recognizes recombinant production of a protein to be production of that particular protein. However, the specification definition refers to further processing. Since the specification definition refers to further processing into another state, the structure of the recombinant molecule is unclear. For example, it is unclear if recombinant human insulin must have the structure of human insulin or if the structure can be modified. Further, since recombinant is defined as 'library of molecules' it is unclear is recombinant insulin, for example, is required to have more than one form of insulin.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin.

Response to Arguments 112 2nd

Since the claims have been amended the rejection has been updated to correspond to the instant claims. Applicants arguments will be considered to the extent that they apply to the instant claims.

Applicants argue (pages 6-7) that the focus should be whether the claim meets the threshold requirements of clarity and precision.

Applicants argue that everything in the specification does not need to be read into the claims.

Applicants argue that the specification clearly defines recombinant to be any type of cloned therapeutic expressed in prokaryotic cells or a genetically engineered molecule.

Applicants argue that it is improper to reject the claim when there is a further definition.

Applicant's arguments filed 8/10/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 6-7) that the focus should be whether the claim meets the threshold requirements of clarity and precision, the focus is whether or not he claims are clear. Since the specification definition (page 26 section 0070) refers to further processing into another state, the structure of the recombinant molecule is unclear. For example, it is unclear if recombinant human insulin must have the structure of human insulin or if the structure can be modified. Further, since recombinant is defined as 'library of molecules' it is unclear is recombinant insulin, for example, is required to have more than one form of insulin.

Although Applicants argue that everything in the specification does not need to be read into the claims, MPEP 2106 expressly states: "Where an explicit definition is provided by the

applicant for a term, that definition will control interpretation of the term as it is used in the claim. Toro Co. v. White Consolidated Industries Inc., 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings."). Any special meaning assigned to a term "must be sufficiently clear in the specification that any departure from common usage would be so understood by a person of experience in the field of the invention." Multiform Desiccants Inc. v. Medzam Ltd., 133 F.3d 1473, 1477, 45 USPQ2d 1429, 1432 (Fed. Cir. 1998). See also MPEP § 2111.01". Thus in the instant case, the definition (page 26 section 0070) controls interpretation. Since the definition is unclear the claims referring to recombinant are unclear. It is consistent with the specification (MPEP 2111) to interpret the term 'recombinant' as it is defined.

Although Applicants argue that the specification clearly defines recombinant to be any type of cloned therapeutic expressed in prokaryotic cells or a genetically engineered molecule, such argument is inconsistent with section 0070 of the specification. The definition recites 'OR' thus each and every possibility is encompassed by the definition. Thus recombinant insulin is a combinatorial library of molecules which may be further processed into another state to form a second combinatorial library. Since the specification definition (page 26 section 0070) refers to further processing into another state, the structure of the recombinant molecule is unclear. For example, it is unclear if recombinant human insulin must have the structure of human insulin or if the structure can be modified.

Although Applicants argue that it is improper to reject the claim when there is a further definition, MPEP 2106 expressly states: "Where an explicit definition is provided by the

applicant for a term, that definition will control interpretation of the term as it is used in the claim. Toro Co. v. White Consolidated Industries Inc., 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999)". Since the definition (page 26 section 0070) includes alternatives (i.e. 'or') each alternative is encompassed by the claim. It is improper to interpret recombinant such that it is not as defined. It appears that applicants have defined a term a certain way, yet expect one to interpret it differently. The definition provided controls interpretation, not what applicants expect one to interpret.

Claim Rejections - 35 USC § 102

Claims were previously rejected under 102 based on the references cited below. Since the claims have been amended the 102 rejections are updated.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27-29,35,41,43-45,47,49,51 are rejected under 35 U.S.C. 102(b) as being anticipated by Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent

claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Although Schroder does not disclose the type of insulin, based on the interpretation of the definition provided for recombinant the insulin of Schroder meets the insulin limitations of claims 43-45,47,49,51.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. The instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph) of certain microparticles. Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder recognize pores in the polymer matrix (page 117 3rd complete paragraph) of certain microparticles. Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

Claims 27-29,35,41,43-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04) as evidenced by Medline (Medline entry from STN for 'Crystallized carbohydrate spheres for slow release and targeting', entered medline Nov 1 1985, 1 page) and Registry (Registry entry for 11061-68-0, entered Nov 16 1984, 1 page).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to

include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Schroder teach insulin. The Medline entry for the Schroder article lists the number 11061-68-0 as the registry number of the insulin (last line). The registry entry for 11061-68-0 recites that the name is human insulin (line 3). As such, Schroder teach human insulin. Since the structure of insulin is the same regardless of whether it is isolated or synthesized the insulin limitations of claims 43-51 are met. In the instant case Medline and Registry are cited as evidence of the identity of the insulin.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531,

535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. The instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph) of certain microparticles. Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder recognize pores in the polymer matrix (page 117 3rd complete paragraph) of certain microparticles. Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

Claims 27-29,35,41,43-45,47,49,51 are rejected under 35 U.S.C. 102(b) as being anticipated by Schroder (US 4,713,249 as cited in IDS 4/21/04).

Schroder (the same author as cited above) teach compositions comprising dextran and insulin (claims 1,4,7). Schroder specifically teach the use of crystallized dextran (abstract, column 2 lines 54-58) which is defined to include hydrogen bonds as recited in claim 27 of the instant invention. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach in

example 13 a specific dextran insulin composition. Schroder teach aqueous solutions (example 13) as recited in claim 28 of the instant invention. Schroder teach that release experiments were performed so a vessel and means is necessarily present (example 13) as recited in claims 29,35 of the instant invention. Schroder teach that insulin is released (example 13). Schroder teach sphere sizes within that of claim 41 of the instant invention (column 5 line 18-20).

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Although Schroder does not disclose the type of insulin, based on the interpretation of the definition provided for recombinant the insulin of Schroder meets the insulin limitations of claims 43-45,47,49,51.

Claims 43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. The instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder teach

(column 2 line 14-17, example 13) release of insulin over time. As such, the microparticles of Schroder do not act as shells since the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder teach (column 2 line 14-17, example 13) release of insulin over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

Response to Arguments 102

Applicants argue (pages 8-15) that the art has not disclosed combining insulin and dextran in the manner presently claimed.

Applicants argue that Schroder teach that the insulin is entrapped in the dextran and that to interpret the claims to not exclude entrapment is wrong and argue that language is parsed from the specification and it is overlooked that claims must be given an interpretation by one possessing ordinary level of skill.

Applicants argue that the instant specification (section 0083) contrasts the present invention from prior art methods and the work of Schroder is the type of composition that is distinguished from the prior art.

Applicants argue that Schroder only teach encapsulation.

Applicants argue that the present claims do not use nonbiodegradable polymer matrices.

Applicants argue that figure 1 of Schroder is a schematic and schematics may add unrealistic elements that aid comprehension and that Schroder does not teach release of insulin from pores. Applicants argue that Figure 1 schematic b shows how the insulin is contained completely within the dextran.

Applicants argue that a specific example is provided at paragraph 0048 that clarifies the structure of the claimed compositions.

Applicants argue that the insulin is enclosed and is not located in pores is borne out at column 2 lines 61-64 of the '249 patent.

Applicant's arguments filed 8/10/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 8-15) that the art has not disclosed combining insulin and dextran in the manner presently claimed, it is noted that although the claims are drawn to products the applicants argue about a method step of 'combining'. Although no process steps are recited in claims 43-45 applicants arguments will be considered. With respect to products made by a process MPEP 2113 states: 'The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983)'.

In the instant case, the office does not have the facility to test and compare the prior art product and the claimed product. However, as set forth in the rejection there is a reasonable basis

that the claim limitations are met. In the instant case, the prior art teach the same components, insulin and crystallized dextran, as in the instant claims. Since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. In the instant case, since Schroder suggest pores in the prior art there is a reasonable basis that the microparticles of Schroder contain pores absence evidence to the contrary. Further, it is noted that the instant application (section 0074) teach that the methods of making are made by any suitable method. Further, Section 2145 I of the MPEP states that arguments of counsel cannot take the place of evidence in the record.

Although Applicants argue that Schroder teach that the insulin is entrapped in the dextran and that to interpret the claims to not exclude entrapment is wrong and argue that language is parsed from the specification and it is overlooked that claims must be given an interpretation by one possessing ordinary level of skill, it is noted that claims 44-45 do not use the word entrap or encapsulate. Claim 43 does use the phrase 'wherein none of the insulin is encapsulated by the porous crystallized dextran microparticle'. The specification (section 0073) states that for a therapeutic agent to not be encapsulated that the microparticle does not act as a shell (it is noted that 'i.e.' means 'that is'). Since MPEP section 2111 states that claims are to be interpreted consistent with the specification one would interpret as expressly recited in section 0073. The specification does not define encapsulation as the equivalent of entrapment.

Further, the art recognizes that entrapment and encapsulation are not equivalents. Lengsfeld (Lengsfeld C 'Introduction to Controlled Drug Delivery' accessed from http://www.engr.du.edu/clengsfe/DrugDelivery.pdf on 10/15/10, 10 pages) teach (slide 5) that

encapsulation involves surrounding drug molecules with a solid polymer shell (and provides a schematic) and teach that entrapment involves the suspension of drug molecules within a polymer matrix (and provides a schematic). It is noted that the Lengsfeld definition of encapsulation is consistent with applicants definition (section 0073) as both refer to a shell. However, entrapment does not require a shell. Entrapment is not the equivalent of encapsulation since encapsulation requires a shell (i.e. a physical barrier) while entrapment does not require a shell. Thus, something that is within a polymer matrix but not within a shell is entrapped but not encapsulated (compare definitions provided by Lengsfeld). A polymer matrix that is porous would not be a solid polymer shell (and would not act to encapsulate). It is noted that Lengsfeld schematic of entrapment is consistent with Figure 1 of Schroder. Thus there is no sidestepping of claim interpretation as asserted by the applicant – the claims have been interpreted consistent with the specification and art-recognized definitions. Further, even if one improperly interpreted encapsulate to be inconsistent with art-recognized definitions, Schroder expressly teach release studies (page 123). In order for the insulin to be released there must necessarily be some type of opening such that the insulin is no longer encapsulated. In other words, at points in time any 'shell' has necessarily been broken. Further, it is noted that as claimed the microparticles are described as porous. One would not recognize porous material as the equivalent of a shell. In the instant case, Schroder recognize that there are pores in the polymer matrix of certain microparticles (page 117 3rd complete paragraph). Further, Schroder teach (Figure 2) that insulin is released over time. As such, there is a reasonable basis that the claim limitations are met, absence evidence to the contrary.

Although Applicants argue that the instant specification (section 0083) contrasts the present invention from prior art methods and the work of Schroder is the type of composition that is distinguished from the prior art, it is first noted that section 0083 of the specification only recites 'All of the publications and patent applications and patents cited in this specification are herein incorporated in their entirety by reference'. Such statement is not a contrast. Perhaps applicants are referring to section 0083 of the PGPub - section 0074 of the specification. It is noted that claims 43-45 are drawn to products and do not recite any specific method steps. Further section 0074 only recites that 'some prior art methods' encapsulate. From such a generic statement one would not be lead to any particular reference. Further, the instant claims do not include any proviso to specifically exclude products of a particular reference. The term 'encapsulated' has not been defined such that one would exclude the work of Schroder.

Although Applicants argue that Schroder only teach encapsulation, it is unclear where Schroder teaches such. Section 2145 I of the MPEP states that arguments of counsel cannot take the place of evidence in the record. Although Schroder refers to entrapment, there is no indication that entrapment is the equivalent of encapsulation. In fact, the art recognize that entrapment and encapsulation are distinct: Lengsfeld (Lengsfeld C 'Introduction to Controlled Drug Delivery' accessed from http://www.engr.du.edu/clengsfe/DrugDelivery.pdf on 10/15/10, 10 pages) teach (slide 5) that encapsulation involves surrounding drug molecules with a solid polymer shell (and provides a schematic) and teach that entrapment involves the suspension of drug molecules within a polymer matrix (and provides a schematic). It is noted that Lengsfeld definition of encapsulation is consistent with applicants definition (section 0073) as both refer to a shell. However, entrapment does not require a shell. Entrapment is not the equivalent of

encapsulation since encapsulation requires a shell (i.e. a physical barrier) while entrapment does not require a shell. In the instant case, there is no evidence that Schroder teaches a shell.

Although Applicants argue that the present claims do not use nonbiodegradable polymer matrices, it is noted that the features upon which applicant relies (i.e., nonbiodegradable polymer matrices) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims recite insulin and crystallized dextran microparticles which are taught by the prior art.

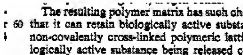
Although Applicants argue that figure 1 of Schroder is a schematic and schematics may add unrealistic elements that aid comprehension and that Schroder does not teach release of insulin from pores that Figure 1 schematic b shows how the insulin is contained completely within the dextran, it appears that applicants argue that conclusions can not be drawn from schematics then applicants go ahead and conclude that insulin is completely within the dextran. Such argumentation is contradictory. MPEP 2113 states: 'The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.

1983)'. In the instant case, the office does not have the facility to test and compare the prior art product and the claimed product. There is no evidence of record to establish a difference between the products. However, as set forth in the rejection there is a reasonable basis that the claim limitations are met.

Although Applicants argue that a specific example is provided at paragraph 0048 that clarifies the structure of the claimed compositions, it is noted that the features upon which applicant relies (i.e., example in the specification) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). MPEP 2106 states: "Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. Toro Co. v. White Consolidated Industries Inc., 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999)". One would not recognize an example as an explicit definition thus the example does not control interpretation.

Although Applicants argue that the insulin is enclosed and is not located in pores is borne out at column 2 lines 61-64 of the '249 patent, for clarity of the record

column 2 lines 59-64 of the '249 patent states


The resulting polymer matrix has such characteristics that it can retain biologically active substances in the non-covalently cross-linked polymeric lattice, the biologically active substance being released concurrently with the slow redissolution of the crystallised carbohydrate matrix.

Instant claim 43 recites 'none of the insulin is encapsulated'. The '249 patent reference to a lattice does not lead one to say that insulin is encapsulated as defined in the instant specification (section 0073) nor would such statement lead one to conclude that insulin is not located in the

pores. In other words, it is unclear how applicants reach the conclusion based on the '249 patent disclosure. It is noted that the word enclosed is not the equivalent of the word encapsulated as defined in the instant specification. The dictionary (Dictionary entry for 'enclose' retrieved from http://dictionary.reference.com/browse/enclose on 10/18/10, 1 page) defines enclose as closing in or surrounding or containing. However, enclose is not defined to require a shell as required by the instant specification definition. In fact, examples of enclose include 'a valley enclosed by tall mountains' and surrounding by a fence. One would not recognize 'a valley enclosed by tall mountains' or being surrounded by a fence as the equivalent of acting as a shell. In other words, to hold or to contain does not mean to act as a shell.

Claim Rejections - 35 USC § 103

Claims were previously rejected under 103 based on the references cited below. Since the claims have been amended the 103 rejections are updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-29,32-33,35,37,41,43-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04) and Moriyama (Journal of Controlled Release 1996 as cited in IDS 4/21/04).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10.

Schroder does not expressly teach PEG as recited in claim 33 in the composition or a composition with a shell as recited in claims 32,37. Schroder does not specify the insulin type.

Moriyama teach (page 238 last paragraph) a solution of PEG and dextran with insulin as recited in instant claim 33. It is noted that in the embodiment of section 2.2 (page 238-239) and section 3.1 (page 240) that there is no cross-linking of the dextran. Moriyama teach that two-phase systems are useful for protein delivery (page 238 column 1). Moriyama teach that insulin will preferentially partition into the PEG phase (page 238 first full paragraph). Moriyama teach that the PEG-dextran two-phase system may exhibit degradation-controlled protein release and prevent drug diffusion (page 238 first column). Moriyama also teach that the compositions were placed in bags (page 239 section 2.5) thus the compositions were necessarily in a shell as recited in claims 32,37 of the instant invention.

Schroder also teach compositions for slow release and targeting (title), specifically with dextran and insulin. One would be motivated to additionally use PEG as taught by Moriyama since Moriyama teach that the PEG-dextran two-phase system may exhibit degradation-controlled protein release and prevent drug diffusion (page 238 first column). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

In the instant case, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of

ordinary skill in the art at the time of the invention. In particular, one would have been motivated to combine the crystallized dextran-insulin composition of Schroder with the PEG component of the composition as taught by Moriyama. Since Moriyama teach that insulin will preferentially partition into the PEG phase (page 238 first full paragraph), the resulting composition meets the limitations of claim 33 of the instant invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Taken together, Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Although Schroder does not disclose the type of insulin, based on the interpretation of the definition provided for recombinant the insulin

of Schroder meets the insulin limitations of claims 43-45,47,49,51. Further, since Schroder teach applications for drug delivery and administration one would be motivated to use human insulin since it is well-known to be used to treat human disease such as diabetes thus meeting the insulin limitations recited in claims 43-51. It is noted that the source of human insulin does not alter the insulin sequence.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. the instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph) of certain microparticles. Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since the insulin is released over time.

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Claims 27-29,32-33,35,37,41,43-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04) and Moriyama (Journal of Controlled Release 1996 as cited in IDS 4/21/04) and Medline (Medline entry from STN for 'Crystallized carbohydrate spheres for slow release and targeting', entered medline Nov 1 1985, 1 page) and Registry (Registry entry for 11061-68-0, entered Nov 16 1984, 1 page).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10.

Schroder does not expressly teach PEG as recited in claim 33 in the composition or a composition with a shell as recited in claims 32,37.

Moriyama teach (page 238 last paragraph) a solution of PEG and dextran with insulin as recited in instant claim 33. It is noted that in the embodiment of section 2.2 (page 238-239) and section 3.1 (page 240) that there is no cross-linking of the dextran. Moriyama teach that two-phase systems are useful for protein delivery (page 238 column 1). Moriyama teach that insulin will preferentially partition into the PEG phase (page 238 first full paragraph). Moriyama teach

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In the instant case, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. In particular, one would have been motivated to combine the crystallized dextran-insulin composition of Schroder with the PEG component of the composition as taught by Moriyama. Since Moriyama teach that insulin will preferentially partition into the PEG phase (page 238 first full paragraph), the resulting composition meets the limitations of claim 33 of the instant invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Taken together, Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Schroder teach insulin. The Medline entry for the Schroder article lists the number 11061-68-0 as the registry number of the insulin (last line). The registry entry for 11061-68-0 recites that the name is human insulin (line 3). As such, Schroder teach human insulin. Since the structure of insulin is the same regardless of whether it is isolated or synthesized the insulin limitations of claims 43-51 are met. In the instant case Medline and Registry are cited as evidence of the identity of the insulin. It is noted that the source of human insulin does not alter the insulin sequence.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and

the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. the instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since there are pores and the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

Claims 27-29,31,35-37,41,43-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04) and Ecanow (US 4,963,526 as cited 11/29/06).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10.

Schroder does not expressly teach the composition in the form of tablets or capsules as in claims 31,36-37.

Ecanow also teach compositions comprising insulin (abstract, claim 1, for example). Ecanow teach that the compositions can be made in the form of tablets (claim 35) as recited in claims 31,36-37.

Since Schroder teach the composition for delivery one would be motivated to obtain the composition in various forms for delivery. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Taken together, Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Although Schroder does not disclose the type of insulin, based on the interpretation of the definition provided for recombinant the insulin of Schroder meets the insulin limitations of claims 43-45,47,49,51. Further, since Schroder teach applications for drug delivery and administration one would be motivated to use human insulin since it is well-known to be used to treat human disease such as diabetes thus meeting the insulin limitations recited in claims 43-51. It is noted that the source of human insulin does not alter the insulin sequence.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. The instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119)

also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since there are pores and the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also shows that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

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Schroder does not expressly teach the composition in the form of tablets or capsules as in claims 31,36-37.

Ecanow also teach compositions comprising insulin (abstract, claim 1, for example). Ecanow teach that the compositions can be made in the form of tablets (claim 35) as recited in claims 31,36-37.

Since Schroder teach the composition for delivery one would be motivated to obtain the composition in various forms for delivery. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Taken together, Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Schroder teach insulin. The Medline entry for the Schroder article lists the number 11061-68-0 as the registry number of the insulin (last line). The registry entry for 11061-68-0 recites that the name is human insulin (line 3). As such, Schroder teach human insulin. Since the structure of insulin is the same regardless of whether it is isolated or synthesized the insulin limitations of claims 43-51 are met. In the instant case Medline and Registry are cited as evidence of the identity of the insulin. It is noted that the source of human insulin does not alter the insulin sequence.

Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. the instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since there are pores and the insulin is released over time.

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Claims 27-30,34-35,41,43-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder (Methods in Enzymology 1985 as cited in IDS 4/21/04) and Clark et al. (US 5,783,556, first cited 1/23/08).

Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10.

Schroder does not expressly teach the composition with instructions as in claims 30,34 Clark teach compositions with insulin (claim 1). Clark further teach kits comprising insulin in which the insulin is in a container (i.e. a vessel) and in which instructions are provided (claim 39) (compare claims 30,34 of the instant invention).

Since Schroder teach the composition for delivery one would be motivated to obtain the composition in various forms for delivery, specifically including instructions for appropriate use and dosage. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Further, it is noted that Section 2112.01 III of the MPEP states that nonfunctional printed matter does not distinguish a claimed product from otherwise identical prior art product.

In relation to the recent KSR decision cited above, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. In particular, one would have been motivated to use the kit and instructions as taught by Clark (who also teaches insulin compositions) with the composition as taught by Schroder thereby meeting the limitations

of claims 30 and 34 of the instant invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Taken together, Schroder teach (page 123 row 1) a composition comprising insulin and crystallized carbohydrate spheres (CCS) which is made from a solution of dextran T10. Thus Schroder teach the components (i.e. insulin and crystallized dextran microparticles) as recited in independent claims 43-45 of the instant invention. Schroder teach that the term crystallization is meant to include hydrogen, and van der Waals interactions, for example (page 119) as recited in claim 27 of the instant invention. Schroder teach aqueous solutions (page 121 last paragraph first sentence, page 122 first paragraph of release studies) as recited in claim 28 of the instant invention. Schroder teach administration via injection (Figure 3 and page 124 last paragraph), so a vessel (such as a syringe) and means is necessarily required thus meeting the limitations recited in claims 29,35 of the instant invention.

Although unclear (see 112 2nd) the term recombinant insulin has been interpreted such that the insulin is required to be some form of insulin. Although Schroder does not disclose the type of insulin, based on the interpretation of the definition provided for recombinant the insulin of Schroder meets the insulin limitations of claims 43-45,47,49,51. Further, since Schroder teach applications for drug delivery and administration one would be motivated to use human insulin since it is well-known to be used to treat human disease such as diabetes thus meeting the insulin

limitations recited in claims 43-51. It is noted that the source of human insulin does not alter the insulin sequence.

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methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. In particular, one would have been motivated to use the kit and instructions as taught by Clark (who also teaches insulin compositions) with the composition as taught by Schroder thereby meeting the limitations of claims 30 and 34 of the instant invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

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Claims 41,43, and 45, for example recite properties (porosity and microparticle diameter) that are not reported by Schroder. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). In the instant case, the claim product and prior art product are substantially identical in composition (i.e. comprise crystallized dextran and insulin) so a prima facie case of anticipation has been established (see MPEP section 2112.01 I).

Claim 43 recites that none of the insulin is encapsulated. the instant specification (section 0073) describes encapsulation as not acting as a shell. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also shows that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. As such, the microparticles of Schroder do not act as shells since there are pores and the insulin is released over time.

Claims 44 and 45 refer to insulin in pores. In the instant case, Schroder recognize pores in the polymer matrix (page 1173rd complete paragraph). Figure 1 (page 119) also suggests that the crystalline polymer matrix has pores. Further, Schroder teach (Figure 2) that insulin is released over time. Thus there is a reasonable basis that the claim limitations are met absence evidence to the contrary.

Response to Arguments 103

Applicants argue (page 15) that Schroder does not teach a composition wherein insulin is located in pores of the crystallized dextran microparticles or a composition wherein none of the insulin is encapsulated.

Applicant's arguments filed 8/10/10 have been fully considered but they are not persuasive.

Although Applicants argue (page 15) that Schroder does not teach a composition wherein insulin is located in pores of the crystallized dextran microparticles or a composition wherein none of the insulin is encapsulated applicants arguments are addressed in the section above entitled 'response to arguments 102'.

Conclusion

Claims were previously rejected under 112 2nd, 102 and 103. Since the claims have been amended the 112 2nd, 102 and 103 rejections are updated.

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654